IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

In re Testosterone Replacement	**)**	
Therapy Products Liability Litigation	**)**	**Case No. 14 C 1748**
Coordinated Pretrial Proceedings	**)**	**MDL No. 2545**
	)	
(This document applies to all cases)	**)**	

CASE MANAGEMENT ORDER NO. 133
(Memorandum Opinion and Order on AbbVie's motion to exclude (1) plaintiffs' general causation opinion testimony in view of studies issued after February 2017, (2) general causation testimony of Dr. Henry Rinder, Dr. Morton Rinder, Dr. Ronald Ziman, and Dr. Douglas Zipes, and (3) supplemental testimony of doctors David Kessler, Peggy Pence, and Martin Wells)

MATTHEW F. KENNELLY, District Judge:

Plaintiffs in this multidistrict litigation (MDL) proceeding allege that they suffered either arterial cardiovascular (CV) injuries or injuries related to blood clots in the veins (venous thromboembolisms) as a result of taking prescription testosterone replacement therapy (TRT) drugs. Defendant AbbVie manufactures AndroGel, one of the TRT products at issue in this litigation.[1] In May 2017, in connection with seven cases involving AbbVie that were selected for bellwether trials, the Court ruled on the parties' *Daubert* and summary judgment motions. *See In re Testosterone Replacement Therapy Prods. Liab. Litig. Coordinated Pretrial Proceedings*, No. 14 C 1748, MDL No. 2545, 2017 WL 1833173 (N.D. Ill. May 8, 2017) ("*CMO 46*"), reconsideration denied, 2017 WL 2953703 (N.D. Ill. July 11, 2017); *In re Testosterone Replacement Therapy Prods. Liab. Litig. Coordinated Pretrial Proceedings*, No. 14 C 1748, MDL No. 2545,

[1] The AbbVie defendants include AbbVie Inc., AbbVie Products LLC, Abbott Laboratories, Inc., Abbott Products, Inc., Unimed Pharmaceuticals, Inc., Solvay Pharmaceuticals, SARL, Solvay Pharmaceuticals, Inc., and Solvay, S.A.

2017 WL 1836435 (N.D. Ill. May 8, 2017); *In re Testosterone Replacement Therapy Prods. Liab. Litig. Coordinated Pretrial Proceedings*, No. 14 C 1748, MDL No. 2545, 2017 WL 1836443 (N.D. Ill. May 8, 2017) ("*CMO 48*").[2] Of the six cases that survived summary judgment, five have been tried to verdict. Plaintiff Cecile Frost's case has yet to be tried, and the Court has ordered a retrial in plaintiff Jeffrey Konrad's case. *See In re Testosterone Replacement Therapy Prods. Liab. Litig. Coordination Pretrial Proceedings*, No. 14 C 1748, MDL No. 2545, 2018 WL 3303269 (N.D. Ill. July 5, 2018).

In 2018, the parties selected six additional cases for bellwether trials in which AbbVie is a defendant. Frost, Konrad, and plaintiffs in the six cases—Gordon Abraham, Dick Bechtholdt, Edwin Harris, George Kibat, Edward Natale, and Dominick Papandrea—allege that AndroGel caused their CV injuries. Their trials are scheduled to take place in October and November 2018.

AbbVie has moved to exclude plaintiffs' expert testimony regarding general causation—that is, whether AndroGel can cause the types of injuries plaintiffs allege they suffered—in light of new evidence AbbVie contends supports its theory of the case. AbbVie has also moved to exclude the general causation opinions of Dr. Henry Rinder, Dr. Morton Rinder, Dr. Ronald Ziman, and Dr. Douglas Zipes. Finally, AbbVie has moved to exclude the supplemental testimony of doctors David Kessler, Peggy Pence, and Martin Wells. For the following reasons, the Court terminates as moot AbbVie's motion to exclude Dr. Henry Rinder's opinion and denies AbbVie's other motions.

Discussion

The Court assumes familiarity with its prior orders, which provide background

[2] CMO stands for Case Management Order.

information regarding this MDL and the cases selected for bellwether trials.

Federal Rule of Evidence 702 governs the admissibility of expert testimony. It provides:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
>
> (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
>
> (b) the testimony is based on sufficient facts or data;
>
> (c) the testimony is the product of reliable principles and methods; and
>
> (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702.

The district court acts as a gatekeeper in determining whether the proposed expert testimony meets the standards of Rule 702. *See Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 597 (1993). The district court's gatekeeping role involves three steps: determining (1) whether the witness is qualified, (2) whether the expert's methodology is scientifically reliable, and (3) whether the testimony will assist the trier of fact to understand the evidence or determine a fact in issue. *See Gopalratnam v. Hewlett-Packard Co.*, 877 F.3d 771, 779 (7th Cir. 2017); *Myers v. Illinois Central R.R. Co.*, 629 F.3d 639, 644 (7th Cir. 2010).

A. AbbVie's motion to exclude all general causation testimony

AbbVie argues that the Court should exclude all of plaintiffs' general causation expert testimony because, it contends, post-February 2017 scientific studies that were not previously before the Court support its theory of the case: there is no causal association between TRT use and CV risk. AbbVie contends that in light of the new

studies, plaintiffs' experts cannot reliably apply the totality-of-the-evidence methodology that the Court has previously ruled is permissible under *Daubert*. AbbVie emphasizes the following language from that ruling: "[E]pidemiology showing a statistically significant association is not an absolute requirement . . . especially in a case where it would be difficult to perform an adequately powered epidemiological study[.]" Defs.' Mot. at 1 (quoting *CMO 46*, 2017 WL 1833173, at *11). The Court understands AbbVie's argument to be twofold. First, AbbVie contends that the new evidence demonstrates that adequately powered studies are *not* difficult to perform, and as a result, plaintiffs' experts must now base their opinions on statistically significant epidemiological studies rather than the totality of the evidence. Second, AbbVie contends that the post-February 2017 scientific studies it cites are unassailable, whereas the studies on which plaintiffs' experts rely in rendering their general causation opinions are flawed. *See, e.g.*, Defs.' Mot. at 3 ("[N]o expert can reliably opine there is general causation in light of [the post-February 2017] studies. . . .").

AbbVie's argument that the post-February 2017 studies confirm its theory, however, is no more authoritative than plaintiffs' argument that it does not. And as plaintiffs point out, one of AbbVie's cited studies states that "[t]here is an ongoing debate in the medical community regarding the effects of testosterone on cardiovascular (CV) health." Defs.' Mot., Ex. G at 1. Now, as before, "it is not the Court's role to choose between competing studies." *CMO 46*, 2017 WL 18833173, at *11. Plaintiffs' general causation experts can continue to offer opinions based on the totality of the evidence, and "the studies' 'merits and demerits . . . can be explored at trial.'" *Id.* (quoting *Schultz v. Akzo Nobel Paints, LLC*, 721 F.3d 426, 433 (7th Cir.

2013)). Recent trial testimony by plaintiffs' expert Dr. Ardehali does not change this conclusion. According to AbbVie, Dr. Ardehali described the post-February 2017 studies as "very substantial." Defs.' Mot. at 3; Defs.' Reply at 1. Dr. Ardehali, however, simply agreed that in general, there is a large body of literature and clinical studies regarding the safety and efficacy of TRTs. *See* Defs.' Mot., Ex. O at 1524:24-1526:3.

AbbVie also faults plaintiffs' experts for failing to address in their supplemental reports each and every post-February 2017 study AbbVie has identified. The failure to do so is not fatal to the experts' opinions because rather than "cherry-pick[] the favorable studies while ignoring unfavorable studies entirely," each expert has explained how newer scientific studies—including some that AbbVie does not identify in its motion—bear on their conclusions. *CMO 46*, 2017 WL 18833173, at *11.[3] Accordingly, the way in which plaintiffs' experts apply the totality-of-the-evidence methodology continues to be reliable, *see id.*, and their general causation opinions are admissible.

B. AbbVie's motion to exclude Dr. Henry Rinder's general causation testimony

AbbVie has moved to exclude Dr. Henry Rinder's general causation opinion from Harris' and Natale's cases. In response, plaintiffs have stated that they inadvertently designated Dr. Rinder as an expert in those cases and have since withdrawn the designation. The Court thus terminates AbbVie's motion as moot.

[3] The Court has previously found that Dr. Halushka's opinion, which focuses only on one biological mechanism, is "reliable even without the consideration of epidemiology." *Id.* at *14 n.12.

C. AbbVie's motion to exclude Dr. Morton Rinder's general causation testimony

Dr. Morton Rinder, a cardiologist, has offered a general causation opinion in Bechtholdt's case.[4] AbbVie does not challenge Dr. Rinder's qualifications but rather argues that he unreliably and inconsistently applies the methodology underpinning his general causation opinion. The Court denies AbbVie's motion.

In his deposition, Dr. Rinder agreed that randomized controlled trials (RCTs) are the "gold standard" for drug safety trials. Defs.' Mot., Ex. A at 110:14-19. He also testified that in general, observational studies are more likely than RCTs to suffer from bias and confounding, and that observational studies can show only "trends." *Id.* at 110:20-111:20; 175:7-176:13. AbbVie argues that Dr. Rinder's methodology is unreliable because, despite this testimony, he (1) fails to identify a clinical trial that reports a risk estimate for heart attacks as a result of TRT exposure, (2) relies on meta-analyses, none of which report a statistically significant increase in such risk, and (3) relies on observational studies. The Court has already addressed virtually identical arguments and has ruled that "an epidemiological study reporting a statistically significant association is not a prerequisite for a reliable causation opinion." *CMO 46*, 2017 WL 1833173, at *11; *cf. id.* at *12 (expert's inability to "quantify the cardiovascular risk he finds in his Bayesian analysis . . . is an issue affecting the weight to be accorded to his analysis, not its admissibility").

Dr. Rinder explains that whether a study informs his opinions depends not on whether it reports statistically significant results, but rather on the soundness of the

[4] Dr. Rinder has also provided a specific causation opinion in Bechtholdt's case, which AbbVie has separately moved to exclude.

study's methodology. *See* Pl.'s Opp., Ex. 2 at 105:23-106:19; Defs.' Mot., Ex. A at 111:1-11. He has "analyzed the existing epidemiological evidence in detail, criticizing the studies on which the other side relies, and drawing different conclusions from the literature." *CMO 46*, 2017 WL 1833173, at *11; *see also, e.g.*, Defs.' Mot., Ex. B (Rinder Report) at 33 (describing the types of evidence he reviewed and why they support his opinion); *id.* at 17-18, 21, 29-30 (explaining that certain studies show statistically significant increases in risk for adverse cardiovascular-related events or surrogate endpoints); *id.* at 19-20, 26-28 (explaining why studies that report no statistically significant relationship between TRT use and risk of adverse cardiac events do not alter his conclusions). Dr. Rinder's agreement during a deposition in a different proceeding that a "weak signal" is not an "established signal" and that AndroGel's ability to cause heart attacks is "neither proven nor unproven" does not undermine his general causation opinion. Defs.' Reply, Ex. A at 161-63. Dr. Rinder has simply acknowledged, as the conflicting scientific evidence suggests, that causation is debated.

AbbVie also argues that Dr. Rinder's reliance on studies that measure surrogate and composite cardiovascular endpoints is inconsistent with his deposition testimony regarding the relevance of such endpoints to the causation question in this case. Dr. Rinder, however, has not opined that these types of endpoints are categorically irrelevant. For example, he explains why a surrogate endpoint in one study cannot reliably measure the risk of heart attacks whereas a surrogate endpoint in another study can. *Compare* Rinder Report at 17 *with id.* at 19-20. Dr. Rinder also explains that certain endpoints can inform a causation analysis where they are adjudicated to be ischemia-related. The fact that Dr. Rinder relies on some studies whose endpoints

were not adjudicated in that manner does not require the Court to exclude his opinion, as he relies on many sources and explains why, in combination, they support his conclusion. *See CMO 46*, 2017 WL 1833173, at *18.

In short, "the proper remedy" for AbbVie's criticisms of Dr. Rinder's methodology "is not exclusion of [his] testimony, but rather testing [it] before the jury using the traditional tools of '[v]igorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof.'" *Id.* at *6 (quoting *Daubert*, 509 U.S. at 596).

D. AbbVie's motion to exclude Dr. Ziman's general causation testimony

Dr. Ziman, a neurologist, has offered general causation opinions for plaintiffs Harris and Natale, who suffered strokes.[5] AbbVie does not challenge Dr. Ziman's qualifications but rather argues that he unreliably applies the totality-of-the-evidence methodology and fails to meet other *Daubert* criteria. As with Dr. Rinder, the Court finds that AbbVie's challenges bear on the weight, rather than the admissibility, of Dr. Ziman's testimony.

First, AbbVie argues that Dr. Ziman's opinion "contradicts current epidemiology"—namely, nine studies published between 2014 and 2017 that report no statistically significant increased risk of stroke associated with AndroGel use. Defs.' Mot. at 5-6. According to AbbVie, Dr. Ziman does not adequately justify his disagreement with these studies. AbbVie also contends that, rather than assess empirical causation based on the presence or absence of statistically significant results, Dr. Ziman uses a "lower threshold . . . based on the principal [sic] that a physician

[5] Dr. Ziman has also offered specific causation opinions for plaintiffs Harris, Natale, and Frost. AbbVie has separately moved to exclude Dr. Ziman's specific causation opinions for Harris and Natale.

should 'do no harm.'" Defs.' Mot. at 5. The Court has already explained why studies that AbbVie contends support its position do not settle the causation debate in this case. Likewise, the Court has explained why general causation experts in this case need not rely on statistically significant results to support their opinions. Having reviewed Dr. Ziman's report and deposition testimony, the Court is satisfied that he has carefully analyzed the scientific literature and has pointed to the "merits and demerits" of supportive and contrary studies. *CMO 46*, 2017 WL 1833173, at *12. For this reason, the Court is unpersuaded by AbbVie's similar argument that Dr. Ziman discounts contrary studies due to certain methodological limitations yet relies on studies subject to the same limitations. *See* Defs.' Mot. at 6-8. The Court also notes that when Dr. Ziman used the phrase "do no harm" during his deposition, he was confirming that his general causation opinion reflects the most accurate conclusion he can draw from his experience and the available data. *See* Pl.'s Opp., Ex. 2 at 111:15-115:22.

AbbVie next argues that Dr. Ziman relies on irrelevant evidence. For example, Dr. Ziman discusses studies regarding hormone replacement therapy in post-menopausal women, injectable TRT, and in vitro animal data, but according to AbbVie, does not adequately explain how the studies inform his opinions and does not account for contrary evidence. The Court is satisfied that Dr. Ziman justifies his reliance on these studies—as have other general causation experts in this case—and notes that Dr. Ziman considers these studies "as part of a much broader set of evidence." *See, e.g.*, *CMO 46*, 2017 WL 1833173, at *13-*14. He explains, for example, how testosterone affects the biological mechanisms at issue in the studies. He also discusses how the evidence finds support in other studies that do observe TRT use in men. *See, e.g.*,

Defs.' Mot., Ex. A (Ziman Report) at 19-20, 36 (discussing how testosterone affects estradiol levels and how estradiol similarly affects men and women). AbbVie also suggests that because the Calof study does not show a statistically significant increase in CV events, it is irrelevant to Dr. Ziman's opinion that TRT can increase stroke risk by increasing hematocrit. But as Dr. Ziman explains, the Calof study is relevant because it shows that TRT increases hematocrit. He uses other evidence to explain why increased hematocrit can cause strokes. *See, e.g.*, Ziman Report at 15-18, 47, 53. AbbVie also faults Dr. Ziman for failing to rely on studies that observe the population on which his opinion focuses: men over the age of sixty-five with pre-existing comorbidities. Dr. Ziman, however, explains why studies observing a wide range of populations and clinical circumstances are probative of his opinion. Like other experts whose general causation opinions this Court has found admissible, Dr. Ziman has "a reliable basis to opine that AndroGel is capable of causing the alleged injuries in the population of TRT users at large." *CMO 46*, 2017 WL 1833173, at *17.

AbbVie's arguments that Dr. Ziman's opinions fail to satisfy other *Daubert* criteria also lack merit. The fact that his opinions are not peer-reviewed and that he has not offered them independent of this litigation do not justify their exclusion. Indeed, at base, AbbVie's contention is that Dr. Ziman has "selectively chose[n] his support from the scientific landscape," Defs.' Mot. at 12 (quoting *In re Rezulin Prods. Liab. Litig.*, 369 F. Supp. 2d 398, 425 & n.164 (S.D.N.Y. 2005))—an argument this Court has already determined is unfounded. AbbVie also assails Dr. Ziman for reaching a conclusion that the Food and Drug Administration (FDA) has allegedly rejected. "[T]he FDA's opinion," however, "is analogous to the opinion of any other expert in this case," and it is up to

the jury "to decide how to weigh the competing expert testimony." *CMO 46*, 2017 WL 1833173, at *13. AbbVie's argument that Dr. Ziman applies different standards in his professional practice is unsupported as well, including because AbbVie does not provide any evidence regarding the number of his patients who use TRT products.

The Court is also unpersuaded by AbbVie's argument that because Dr. Ziman does not provide evidence of a dose-response relationship, he cannot opine that AndroGel was a substantial factor in causing a plaintiff's injuries. Dr. Ziman does discuss how certain studies suggest that higher doses of AndroGel pose greater CV risks. *See, e.g.*, Ziman Report at 25-27, 53 (discussing Christou 2016, Basaria 2013, Ferenchick 1990, 1992). Furthermore, the Court has not required general causation experts in this MDL to discuss whether specific AndroGel doses are associated with CV risks. After AbbVie argued in 2017 that the Court should exclude causation opinions that fail to do so, the Court determined that "a causation opinion based on the totality of the evidence" need not address "each Bradford Hill factor"—one of which is a dose-response relationship. *CMO 46*, 2017 WL 1833173, at *9, *11. And the Court found that the evidence on which plaintiffs' experts relied, including many of the studies that Dr. Ziman discusses, provide a sufficient basis from which to opine that AndroGel can cause the alleged injuries "in the population of TRT users at large." *Id.* at *17.

AbbVie's cited cases do not persuade the Court to alter this ruling, including because none holds that an expert must always provide evidence of a dose-response relationship. *See In re Lipitor (Atorvastatin Calcium) Marketing, Sales Practices & Prods. Liab. Litig.*, 174 F. Supp. 3d 911, 917-19 (D.S.C. 2016) (where plaintiffs allege that four commercially available doses of Lipitor caused their injuries and there is

"evidence that an association no longer holds at low doses," including one of the doses at issue, experts must provide dose-specific causation reports); *see also In re Lipitor (Atorvastin Calcium) Marketing, Sales Practices & Products Liab. Litig.*, 892 F.3d 624, 640 (4th Cir. 2018) ("*Lipitor II*") ("We do not suggest that every case involving a claim of injury resulting from a pharmaceutical drug will require a dose-by-dose analysis, and an expert witness will not necessarily need to define the precise lower bound of exposure risk."); *Rezulin*, 369 F. Supp. 2d at 427 (court excluded expert reports because experts had "offered no evidence" that their causation theory "was possible"). The circumstances in the *Lipitor* cases are not present here, and Dr. Ziman has provided sufficient evidence to suggest that his causation theory is scientifically possible.

Finally, AbbVie is incorrect that Dr. Ziman's methodology is unreliable because he applies the Bradford Hill criteria without first establishing an association between AndroGel use and CV risk "through studies with statistically significant results." Defs.' Reply at 1 (quoting *Lipitor II*, 892 F.3d at 640). Unlike the expert in *Lipitor II*, whom the court faulted for failing to follow this two-step process, 892 F.3d at 642, Dr. Ziman does not base his general causation opinion solely on the Bradford Hill criteria. Rather, consistent with this Court's prior orders, he opines based on the totality of the evidence. *See CMO 46*, 2017 WL 1833173, at *9-*10. As the Court has explained, Dr. Ziman may consider Bradford Hill factors as part of that analysis. *Id.* at *11. But he need not proffer evidence of a statistically significant association before doing so, nor must he address every Bradford Hill factor. *Id.*

For all of these reasons, Dr. Ziman's general causation opinion satisfies the standards of Rule 702 and *Daubert*. AbbVie will have the opportunity on cross-examination to question Dr. Ziman about the alleged weaknesses in his analysis.

E. AbbVie's motion to exclude Dr. Zipes' general causation testimony

Dr. Zipes, a cardiologist with training in electrophysiology, has offered general causation opinions for plaintiffs Abraham, Bechtholdt, Kibat, and Papandrea. AbbVie argues that Dr. Zipes unreliably applies the totality-of-the-evidence methodology and that he is not qualified to offer certain opinions. The Court denies AbbVie's motion.

First, AbbVie argues that Dr. Zipes fails to adequately explain why he disagrees with the "growing body" of contrary studies. Defs.' Mot. at 4. Similarly, AbbVie faults Dr. Zipes for failing to address some of these studies. And AbbVie highlights deposition testimony in which Dr. Zipes acknowledged he was unaware of certain contrary studies. Dr. Zipes, however, analyzes at least five of the studies AbbVie identifies. *See* Defs.' Mot., Ex. A (Zipes Report) ¶¶ 89, 99, 100, 101, 201. Like Dr. Ziman, Dr. Zipes discusses "merits and demerits" of studies that support and contradict his opinion. *CMO 46*, 2017 WL 1833173, at *12; *see, e.g.*, Zipes Report ¶ 92 (discussing limitations of the Vigen 2013 study). The fact that Dr. Zipes does not discuss every study AbbVie views as relevant, or that he may have overlooked a study, does not mean that he unreliably applies his methodology. The Court notes that AbbVie ignores plaintiffs' argument that an AbbVie expert, Dr. French, has not discussed a study that plaintiffs consider relevant and has failed to discuss all of the studies AbbVie argues Dr. Zipes should have discussed.

AbbVie also argues that Dr. Zipes relies on irrelevant information to "skew[]" the body of evidence in his favor. Defs.' Mot. at 5. This information includes studies regarding the use of estrogen and progestin in post-menopausal women and high-dose steroids, and studies using in vitro animal data. Similarly, AbbVie criticizes Dr. Zipes' conclusions regarding hematocrit as a biologically plausible mechanism because he does not identify statistically significant evidence that increased hematocrit resulting from TRT use is associated with heart attacks. These criticisms are nearly identical to those that AbbVie launched against Dr. Ziman. The Court finds that like Dr. Ziman, Dr. Zipes provides an adequate basis to explain why the disputed evidence supports his opinion.

In addition to arguing that Dr. Zipes relies on irrelevant information, AbbVie argues that he inconsistently weighs evidence, including by relying on observational studies despite acknowledging their methodological limitations. As with Dr. Ziman, however, Dr. Zipes explains why variability in observational studies is to be expected, s*ee* Zipes Report ¶ 91; does not rely solely on observational studies; and adequately grounds his opinion in the totality of the evidence. AbbVie emphasizes Dr. Zipes' admission that he fails to address one study that may reveal flaws in the Xu meta-analysis, and that in a textbook he co-authored, he did not list TRT among all "known" causes of CV events. Defs.' Mot. at 12-13. None of these alleged flaws render Dr. Zipes' methodology unreliable; rather, they are all matters of weight.

Next, according to AbbVie, Dr. Zipes opines that "any dose" of AndroGel can cause a heart attack. Defs.' Mot. at 15. The Seventh Circuit, AbbVie contends, has rejected this theory. *Id.* (citing *Krik v. Exxon Mobil Corp.*, 870 F.3d 669 (7th Cir. 2017)).

But as in *Lipitor* and *Rezulin*, the court in *Krik* did not hold that an expert must always identify the specific dose of a drug that is necessary to cause the alleged response. In *Krik*, plaintiff alleged that he developed lung cancer due to asbestos exposure. 870 F.3d at 674. His expert opined that "each and every exposure to asbestos, including the first exposure, no matter how de minimis," was a substantial contributing factor in causing plaintiff's cancer. *Id.* at 674-75. The expert also admitted he had "not considered any information about amount of exposure in [his] analysis." *Id.* at 675. The court, having already found that "asbestos-induced cancer is dosage dependent," concluded that the "de minimis" exposure theory did not satisfy the standards of Rule 702 and *Daubert*. *Id.* at 675-77. But unlike the expert in *Krik*, Dr. Zipes has provided only a general causation opinion. Furthermore, Dr. Zipes' opinion is based on studies that observe AndroGel in doses that patients actually take, rather than in "de minimis" doses. *See, e.g.*, Zipes Report ¶¶ 56, 69-70. And although Dr. Zipes testified at one point during his deposition that AndroGel can increase heart attack risk "regardless of dose," the context makes clear that he does not purport to opine that a "very tiny amount of AndroGel" is sufficient to do so. *See* Defs.' Mot., Ex. B at 62:6-63:12. Dr. Zipes' dose-related statements do not render his opinion unreliable; rather they affect only its weight.

AbbVie's final argument is that Dr. Zipes is not qualified to opine about the scope of AndroGel's indications or about whether clinical trials have adequately established AndroGel's safety and efficacy for treating age-related hypogonadism. The Court disagrees. Although Dr. Zipes does not claim to have FDA regulatory experience or direct involvement in drug safety testing, he has more than forty years of experience as

a practicing cardiologist; is a professor of medicine, pharmacology, and toxicology; and has served on editorial boards of several medical journals. Based on this experience, Dr. Zipes is more than capable of interpreting AndroGel's label, assessing AndroGel's testing to date, and communicating that FDA-mandated testing has not been completed. AbbVie contends that this last statement misleadingly omits information about the status of the testing, but AbbVie can address this issue on cross-examination. The Court does, however, reserve its right to exclude as cumulative the opinions in paragraph 105 of Dr. Zipes' report if plaintiffs designate experts that offer duplicative overlapping testimony—as it does with any expert offered by either side.

F. AbbVie's motion to exclude the supplemental testimony of Drs. Kessler, Pence, and Wells

1. Dr. Kessler

Dr. Kessler is a former commissioner of the FDA. In his original expert report and in testimony at bellwether trials, he has offered opinions regarding the FDA's role in regulating drugs; its role in regulating branded and unbranded drug advertisements; and factors one should consider in determining whether a company is marketing and promoting its drug for approved uses. AbbVie has moved to exclude the first and second addenda to Dr. Kessler's report.

In the first addendum, AbbVie takes issue with Dr. Kessler's statements that unbranded advertisements "were linked, as a matter of strategy, to branded ads that advertised AndroGel" and that "[t]he effect of this strategy . . . was to promote AndroGel for off-label indications for which the safety and efficacy was not established." Defs.' Mot. at 1 (quoting Defs.' Mot., Ex. A ¶ 4). According to AbbVie, these statements violate the Court's prior ruling that Dr. Kessler "cannot offer an opinion or conclusion about

what AbbVie intended." *CMO 48*, 2017 WL 1836443, at *15. The Court disagrees. As it has previously explained, Dr. Kessler may "evaluate[] AbbVie's marketing materials and internal memoranda to assess whether and to what extent it was targeting persons with conditions outside of AndroGel's indicated use." *Id.* He may also "offer[] a framework by which the jury can assess what AbbVie intended via its marketing." *Id.* The opinions AbbVie challenges fall squarely into these categories, and Dr. Kessler's use of the words "strategy" and "effect" do not convert them into conclusions about AbbVie's state of mind. AbbVie's objection that Dr. Kessler's opinions are speculative is also unfounded, as Dr. Kessler's original report and the first addendum cite numerous documents tending to support his opinions. The opinions in the first addendum are "based on sufficient facts or data." Fed. R. Evid. 702; *see, e.g.*, *CMO 48*, 2017 WL 1836443, at *13-*15. Finally, AbbVie's arguments that Dr. Kessler does not use a reliable methodology and is not qualified to offer his opinions are without merit. *See id.* at *13-*14 (in response to similar arguments, explaining why Dr. Kessler's "professional experience provides him with a wealth of knowledge that he appropriately may draw upon in forming his opinions for this case").

Regarding the second addendum, AbbVie contends that Dr. Kessler improperly opines on AbbVie's state of mind by "insinuat[ing]" that AbbVie paid reprint fees to the Endocrine Society with the intent to influence its published TRT treatment guidelines. Defs.' Mot. at 2. The second addendum, however, contains no such opinion. It instead describes facts from which a jury could, but need not, draw this inference. AbbVie also argues that Dr. Kessler is not qualified to opine that the Endocrine Society is "not a 'legitimate' research organization." *Id.* at 4. Again, however, Dr. Kessler does not

actually offer this opinion in his addendum. AbbVie's argument that Dr. Kessler's opinions about conflicts of interest are speculative likewise lacks merit because he describes facts tending to support them. If AbbVie wishes to challenge the substance of the opinions, it can do so through cross-examination. Finally, AbbVie argues that Dr. Kessler's testimony merely adds "gloss" to several subjects and will not assist the jury. Defs.' Mot. at 5; Defs. Reply at 3. The Court has previously rejected a nearly identical argument, finding that Dr. Kessler's testimony would assist the jury without impeding its fact-finding role. *See CMO 48*, 2017 WL 1836443, at *15. The same is true here.

Overall, the challenged opinions in Dr. Kessler's first and second addenda meet the requirements of Rule 702 and *Daubert*. They are also relevant and do not invade the jury's province. Their probative value, therefore, is not substantially outweighed by the risk of prejudice. *See* Fed. R. Evid. 403.

2. Dr. Pence

Dr. Pence has an advanced degree in toxicology and pharmacology. She is an expert in pharmaceutical regulatory affairs and interactions with the FDA. In an expert report and in testimony at bellwether trials, Dr. Pence has offered opinions on these topics as they relate to AndroGel.

AbbVie now moves to exclude Dr. Pence's opinion that "[i]t has been estimated that 'FDA receives by direct report less than 1% of suspected serious' adverse drug reactions." Defs.' Mot., Ex. E ¶ 1 (citation omitted). AbbVie argues that Dr. Pence's methodology in reaching this opinion is unsound, including because she relies on a decades-old article whose data she could not locate, and admits that she could not confirm exactly how the article defines "direct report." Defs.' Mot. at 6. AbbVie also

moves to exclude Dr. Pence's opinion that the underreporting rate can be "as high as 100%." Defs.' Mot., Ex. E ¶ 3. AbbVie emphasizes that this opinion is based on only one of thirty-seven studies in the article Dr. Pence cites for support, and that Dr. Pence does not discuss the remaining studies. Dr. Pence, however, has previously testified at trial—without objection—that "some estimates say that fewer than 1 percent of actual events get reported." *See* Pls.' Opp., Ex. 12 at 1864:21-1865:6. AbbVie's challenges to Dr. Pence's supplemental opinions regarding the underreporting rate involve matters of weight rather than admissibility. *See CMO 48*, 2017 WL 1836443, at *13.

AbbVie also argues that in citing trial testimony by an AbbVie witness, Dr. Pence improperly opines about what AbbVie "believes" is the underreporting rate. *See* Defs.' Mot. at 8. This argument is frivolous. Dr. Pence cites testimony that an AbbVie witness has twice offered at trial as one piece of evidence in support of her own conclusions. And although AbbVie complains that Dr. Pence mischaracterizes the testimony, it does not point to any mischaracterization, and the Court sees none. The opinions in Dr. Pence's supplemental report are admissible, and AbbVie is free to address their purported flaws through cross-examination.

3. Dr. Wells

Dr. Wells is a biostatistician. He has previously offered expert opinions in this case regarding the statistical power of studies that observe the potential association between TRT use and CV risk. AbbVie argues that in his supplemental report, Dr. Wells unreliably applies Bayesian statistics in analyzing two epidemiological studies. AbbVie complains that Dr. Wells' method is unreliable because his results differ from the conclusions of the underlying studies which, using frequentist statistical methods, report

no statistically significant association. AbbVie, however, has not explained how Dr. Wells' methodology is any different from that of Dr. Gerstman, whose Bayesian critiques of epidemiological studies the Court has previously found admissible under *Daubert*. *See CMO 46*, 2017 WL 1833173, at *12. AbbVie does contend that Dr. Wells fails to explain why he re-analyzes some studies and not others, but this is a matter of weight and does not warrant exclusion of Dr. Wells' testimony. *See, e.g.*, *id.* at *6.

Conclusion

For the foregoing reasons, the Court denies AbbVie's motion to exclude plaintiffs' general causation opinion testimony in view of studies issued after February 2017 [dkt. no. 2737]; terminates as moot AbbVie's motion to exclude Dr. Henry Rinder's general causation testimony [dkt. no. 2732]; denies AbbVie's motion to exclude the general causation testimony of Dr. Morton Rinder [dkt. no. 2738], Dr. Ziman [dkt. no. 2743], and Dr. Zipes [dkt. no. 2742]; and denies AbbVie's motion to exclude supplemental testimony of doctors Kessler, Pence, and Wells [dkt. no. 2733].

MATTHEW F. KENNELLY
United States District Judge

Date: August 23, 2018